REMARKS

Claims 1-15, 18, and 22-24 are pending.

Claims 1-15 and 22 are allowed.

Claims 3, 18, 23 and 24 are amended herein. The amendments are supported by the specification and do not contain new matter.

Claims 18, 23 and 24 are rejected as unenabled or indefinite under 35 U.S.C. §112. For reasons to be set forth below, and in view of amendments made herein, Applicants assert that the claims are allowable.

1. Claim 18 Is Enabled

Claim 18 is rejected under 35 U.S.C. §112, first paragraph, because, according to the Examiner:

> the specification, while being enabling for introducing a nucleotide sequence into target cells *in vitro* or *in vivo* for the expression [of] a nucleotide sequence specifically encoding a marker gene, does not reasonably provide enablement for introducing *any* nucleotide sequence into *any* target cell.

The Examiner contends that "introducing genes for therapeutic purposes is not enabled because of the deficiencies surrounding gene therapy practices", citing Verma et al., *Nature* **389**:239-242 (1997). The Examiner further refers to the following citations:

> In addition, a review by Anderson (*Nature* **392**:25-30, 1998, see entire document) focuses on the promise and problems specifically facing human gene therapy using retroviral vectors, pointing out that the "problems that investigators face in developing retroviral vectors that are effective in treating disease are of four main types: obtaining efficient delivery, transducing non-dividing cells, sustaining long-term gene expression, and developing a cost-effective way to manufacture the vector" . . . . Furthermore, it has been established that "results of clinical trials have been disappointing" because "[E]ven the most successful trial has fallen short of therapeutic efficacy." Kmiec, *American Scientist* **87**:240-247, 1999).

Applicants assert that claim 18, as amended, is fully enabled. The object of the claimed method is to "introduce a nucleotide sequence into target cells". Some of the statements provided as basis for the rejection suggest that the Examiner is regarding

the claims as "methods of treatment by gene therapy", which they are not. Regardless of the utility that Applicants ascribe to their claimed retroviral vectors for use in gene therapy, the ability of the claimed vectors to introduce a gene into a target cell could be used for other purposes. For example, the claimed vectors could be used to introduce a toxic gene to ablate target cells in order to produce disease model systems. The claimed vectors would be particularly useful for this purpose, as the nature of the construct, where promoter and coding sequence are physically separated in antisense orientation, prevents expression of the toxic gene in the packaging cell line, thereby improving viral yields. In addition, the claimed vectors, carrying a marker gene, could be used to identify cells within a larger population that are permissive for retroviral infection, thereby providing an index of the likelihood of success of retroviral-mediated gene therapy within the cell population.

Accordingly, the enablement standard should be applied to the step of *introducing* a gene of interest, not the ultimate objective of said introduction - a number of *bona fide* objectives exist beyond gene therapy. In this regard, Applicants assert that the specification enables the introduction of genes of interest by the disclosed vectors. Further, successful introduction is demonstrated by the working examples. There is no reason to believe that introduction of the *egfp* gene would *not* be representative of introduction of any other gene that could be contained in the virus. Even if, for the sake of argument, some exceptions were to exist, not all possible embodiments of a claim are required to be operable.

To more clearly set forth that the focus of claim 18 is introduction of a gene of interest, Applicants have amended claim 18 to include features associated with successful infection, where infection necessarily introduces the gene of interest into the target cells. In particular, the claim is amended to provide that the target cells are susceptible to infection by the administered retrovirus, and that an infective amount of retrovirus is used.

In view of these amendments and remarks, Applicants request that the rejection be withdrawn.

2. The Amended Claims Are Not Indefinite

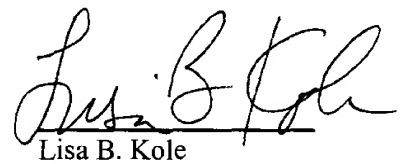
Claims 23 and 24 are rejected as indefinite under 35 U.S.C. §112, for reciting "said one or more sequences" without providing adequate antecedence.

As suggested by the Examiner, the claims have been amended to recite "said one or more *coding* sequences", thereby obviating the basis for the rejection. Claim 3 has been similarly amended.

3. Conclusion

For all the foregoing reasons, Applicants request that the rejections be withdrawn and that all claims be allowed to issue. An early allowance is earnestly requested.

Respectfully submitted,



Lisa B. Kole
PTO Reg. No. 35,225
(212) 408-2628

BAKER BOTTS, L.L.P.
30 Rockefeller Plaza
New York, NY 10112

ATTORNEYS FOR APPLICANTS